Paper XII Studies on the Metabolism of Fission Products IV. The Effects of EDTA-Na upon the Metabolism of Radiostrontium and Radioyttrium in Mice (The Radioactive Dust from the Nuclear Detonation)

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PAPER XII

Studies on the Metabolism of Fission Products
IV. The Effects of EDTA-Na upon the Metabolism of Radiostrontium and Radioyttrium in Mice

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INTRODUCTION

Decontamination studies of internally deposited radioelements are considered to be an important problem in the prevention and treatment of radiation hazards due to fission products. The influence of EDTA, sodium and zirconium citrates, parathormone, and sulfhydryl compounds, cysteine and 2,3 dimercaptopropanol (BAL) upon the metabolism of certain fission products and plutonium has been studied by several investigators. [1,2,3,4,5,6] This paper is concerned with the study of the effect of EDTA-Na upon the metabolism of radiostrontium, radioyttrium and rare earth group in mice. In addition to this the toxicity of EDTA, and inert strontium and barium in mice has been studied.

MATERIALS, METHODS, AND RESULTS

1) The toxicity of EDTA-Na.

The EDTA-Na ($C_{10}H_{12}O_8N_2Na_4$) used was the product of the Tokyo Chemical Engineering Co. The EDTA-Na was dissolved in physiologic saline solution in various concentrations ranging from 0.01 to 5.0 per cent. After sterilization by heating, 0.5 cc. or 1.0 cc. of the solution of each concentration was injected subcutaneously in the back of 2 to 5 mice weighing from 10 to 15 grams, and the toxicity was observed for 12 days. The results are summarized in Table 1.

2) The effects of EDTA-Na upon the distribution of radiostrontium, radioyttrium and rare earth group in mice.

In the back of adult mice weighing 12 to 16 grams, 0.25 cc. of physiologic saline solution of $Sr^{89,90}$ or Y^{91}, or 0.5 cc. of the fraction of the rare earth group was injected subcutaneously together with 0.25 cc. of 1 per cent physiologic saline solution of EDTA-Na. As the controls, the same dose of the radiostrontium, or radioyttrium or the rare earth group was injected subcutaneously in the back of adult mice weighing 12 to 16 grams together with 0.25 cc. of physiologic saline solution. Five mice were used in each experiment. The radiostrontium used was supplied by

Table 1. The toxicity of EDTA-Na

	Concentration (%)	Dose (cc.)	Dose (mg.)	EDTA-Na (mg./gr. body weight)	Death
(1)	0.01	0.5	0.05	0.005	0/5
(2)	1.0	0.5	5	~ 0.5	0/5
(3)	1.0	1.0	10	~ 1.0	0/2
(4)	3.0	0.5	15	~ 1.5	5/5
(5)	4.0	0.5	20	~ 2.0	5/5
(6)	5.0	0.5	25	~ 2.5	3/3

(1) 0.01%, 0.5cc, (5 mice) : No symptom was observed. All animals survived.
(2) 1.0%, 0.5cc. (5 mice) : The animals were excited for 30 minutes following the injection. Thereafter no symptom was observed and all animals survived.
(3) 1.0%, 1.0cc. (2 mice) : The results were the same as (2).
(4) 3.0%, 0.5cc. (5 mice) : The animals were excited for 5 minutes following the injection. About 16 minutes after the injection the animals became less energetic, and 2 out of 5 animals showed convulsions 16 to 18 minutes after the injection and died within one hour. The other three could not walk and died within 10 to 40 hours following the injection.
(5) 4.0%, 0.5cc. (5 mice) : The animals were excited for 5 minutes following the injection. Thereafter they became less energetic, and one of them developed convulsions 8 minutes after the injection and died 20 minutes after the injection. The other four became motionless within 30 minutes after the injection and died within 3 hours.
(6) 5.0%, 0.5 cc. (3 mice) : After temporary excitement the animals became less energetic. Then they developed convulsions and all died within one hour after the injection.

the U. S. AEC. The radioyttrium and rare earth group were separated from the radioactive ashes collected from the No.5 Fukuryu Maru as described in the previous paper.[7]

Four hours following the injection the animals were sacrificed and the liver, lungs, spleen, kidneys, blood, digestive tract (including the stomach, small and large intestines together with their contents) and bones (both femurs, tibias and fibulas, including the bone marrow) were removed. After weighing, the samples were wet ashed with perchloric acid and hydrogen peroxide, transferred in glass dishes 3 cm. in diameter, dried, and the radioactivity was measured with a Geiger-Mueller counter. The results are shown in Table 2 and Figures 1, 2, 3.

The deposition of radiostrontium in the tissues examined showed a tendency to decrease in case of the simultaneous injection of $Sr^{89,90}$ and EDTA-Na as compared with the controls. This tendency was especially marked in the bones. The difference, however, was not statistically significant. In case of Y^{91}, the deposition of radioyttrium in the bones was also decreased following the simultaneous injection of Y^{91} and EDTA-Na as compared with the controls. The decrease of the deposition of Y^{91} in the bones following the simultaneous injection of Y^{91} and EDTA-Na was more marked than that of $Sr^{89,90}$. The difference, however, was not statistically significant. In case of the rare earth group separated from the radioactive ashes,

Table 2. The effects of EDTA-Na on the distribution of $Sr^{89,90}$, Y^{91} and rare earth group in the tissues of the mouse (4 hours following subcutaneous injection)

		$Sr^{89,90}$ and EDTA-Na	$Sr^{89,90}$ and saline	Y^{91} and EDTA-Na	Y^{91} and saline	Rare earth group and EDTA-Na	Rare earth group and saline
Liver	p. w. o.	0.23±0.046	0.83±0.11	0.28±0.08	0.37±0.09	0.08±0.01	0.09±0.036
	p. g. t.	0.29±0.09	1.38±0.13	0.55±0.20	0.67±0.39	0.17±0.03	0.12±0.02
Spleen	p. w. o.	0.02±0.002	0.02±0.003	0.02±0.007	0.00±0.00	0.04±0.02	0.00±0.00
	p. g. t.	0.17±0.04	0.35±0.05	0.18±0.06	0.00±0.00	0.55±0.24	0.00±0.00
Lung	p. w. o.	0.06±0.004	0.12±0.02	0.06±0.02	0.01±0.007	0.01±0.003	0.01±0.002
	p. g. t.	0.41±0.03	1.12±0.24	0.43±0.16	0.07±0.04	0.06±0.03	0.05±0.021
Digest. tract	p. w. o.	2.71±0.48	2.93±0.39	0.33±0.07	2.52±1.83	0.12±0.04	5.14±2.205
	p. g. t.	1.01±0.15	1.05±0.18	0.14±0.05	1.31±0.90	0.06±0.02	2.29±1.37
Blood	p. g.	0.38±0.08	0.90±0.29	0.44±0.21	0.18±0.14	0.17±0.02	0.10±0.06
Kidney	p. w. o.	0.13±0.02	0.32±0.026	0.57±0.31	0.16±0.09	0.16±0.108	0.10±0.05
	p. g. t.	0.58±0.06	0.72±0.05	2.56±1.56	1.15±0.73	0.86±0.53	0.52±0.25
Bone	p. w. s.	2.00±0.19	2.67±0.32	0.29±0.07	2.98±1.26	0.21±0.109	0.89±0.29
	p. g. t.	10.32±1.58	19.64±4.12	1.50±0.45	10.78±4.70	0.67±0.37	4.35±0.82

p. w. o. per whole organ
p. g. t. per gram tissue
p. g. per gram
p. w. s. per whole sample (both femurs, tibias and fibulas)

Values are presented as group means of the percent of the administered dose ± the standard error of the mean.

Fig. 1. Effect of EDTA-Na on the distribution of $Sr^{89,90}$ in the tissues of the mouse 4 hours following subcutaneous injection (per gram).

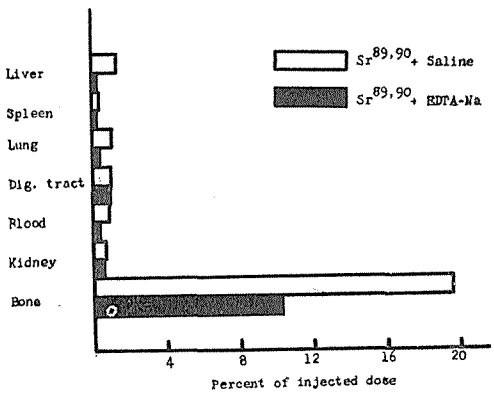
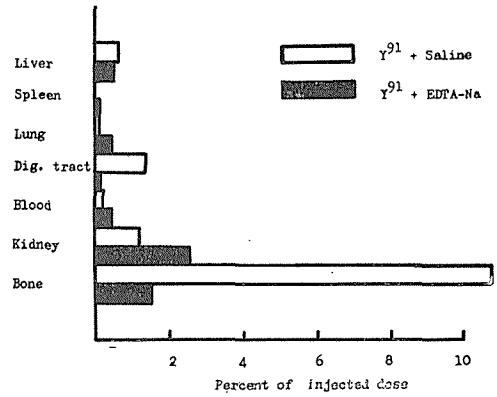


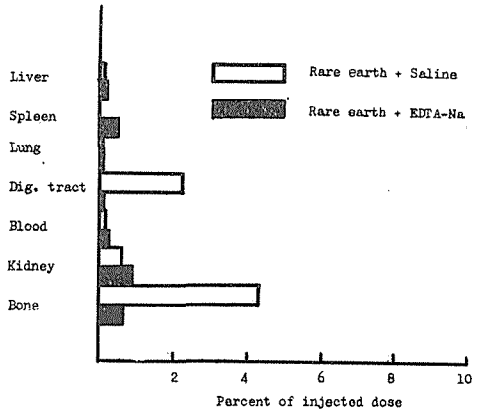
Fig. 2. Effect of EDTA-Na on the distribution of Y^{91} in the tissues of the mouse 4 hours following subcutaneous injection (per gram).



the deposition of the elements of the rare earth group in the bones was decreased following the simultaneous injection of the rare earth group and EDTA-Na as

compared with the controls, and the difference was statistically significant.

Fig. 3. Effect of EDTA-Na on the distribution of rare earths in the tissues of the mouse 4 hours following subcutaneous injection (per gram).



3) The toxicity of strontium nitrate.

Strontium nitrate was dissolved in physiologic saline solution in various concentrations ranging from 0.1 to 10.0 per cent. In the back of mice weighing 6 to 12 grams, 0.5 cc. of the solution of each concentration was injected subcutaneously, and the toxicity was observed. The results are summarized in Table 3.

Table 3. The toxicity of strontium nitrate

Concentration(%)	Dose (cc.)	Dose (mg.)	Strontium nitrate mg./gr. body weight	Death	Remarks
0.1	0.5	0.5	0.063	0/3	No symptom.
0.5	0.5	2.5	0.313	0/5	〃
1.0	0.5	5.0	0.625	0/5	〃
2.0	0.5	10.0	1.250	1/5	Became less energetic 2 hrs. after the injection.
3.0	0.5	15.0	1.875	4/5	Death occurred within 12 hrs. after the injection.
4.0	0.5	20.0	2.500	5/5	〃 〃
5.0	0.5	25.0	2.500	5/5	〃 〃
10.0	1.0	100.0	10.000	5/5	Death occurred within 90 min. after the injection.

4) The toxicity of barium nitrate.

Barium nitrate was dissolved in physiologic saline solution in various concentrations ranging from 0.2 to 1.0 per cent. In the back of mice weighing 6 to 12 grams, 0.5 cc. of the solution of each concentration was injected subcutaneously, and the toxicity was observed. The results are summarized in Table 4.

Table 4. The toxicity of barium nitrate

Concentration(%)	Dose (cc.)	Dose (mg.)	Barium nitrate mg./gr. body weight	Death	Remarks
0.2	0.5	0.10	0.013	0/5	Became less energetic 1 hour after the injection. Recovered 2 hours after the injection.
0.3	0.5	0.15	0.018	1/5	One died 25 min. after the injection. The other became motionless 1 hour after the injection. Recovered after 3 hours.
0.5	0.5	0.25	0.020	5/5	Excited immediately after the injection. Death occurred within 2 hours.
1.0	1.0	1.00	0.080	5/5	Excited immediately after the injection. Death occurred within 40 min.

DISCUSSION

Cohn and Gong[6] have studied the effect of ethylendiamine-tetraacetic acid (EDTA) on skeletal content and excretion of injected radiostrontium in rats. According to their report, administration of salts of EDTA under the most favorable conditions for its action had no effect upon skeletal distribution of injected carrier free Sr^{89}. In our experiments, simultaneous injection of EDTA-Na had no statistically significant effect upon the distribution of injected radiostrontium in mice. However, when EDTA-Na was injected simultaneously with rare earth elements, the deposition of the elements in the bones was decreased as compared with the controls. From these results it might be concluded that simultaneously injected EDTA-Na lowers the distribution of the rare earth elements in the bones in mice.

SUMMARY

1) The effects of EDTA-Na upon the metabolism of radiostrontium, radioyttrium and rare earth group have been studied in mice. The radioyttrium and rare earth group used were separated from the radioactive ashes collected from the No. 5 Fukuryu Maru.

2) The toxicity of EDTA-Na, inert strontium nitrate and barium nitrate has been studied.

3) Simultaneous injection of EDTA-Na showed no significant effect upon the distribution of radiostrontium in the bones of mice.

4) The distribution of radioyttrium in the bones of mice tended to decrease

following the simultaneous subcutaneous injection of Y^{91} and EDTA-Na as compared with the controls.

5) There was a statistically significant decrease in the distribution of the rare earth group separated from the radioactive ashes collected from the No. 5 Fukuryu Maru in the bones of mice as compared with the controls.

6) The mice given more than 1.5 mg. of EDTA-Na per gram body weight by subcutaneous injection could not survive.

7) Following subcutaneous injection of less than 0.625 mg. of strontium nitrate per gram body weight all mice survived. Some of the mice died following subcutaneous injection of 1.250 mg. of strontium nitrate per gram body weight. Following subcutaneous injection of more than 2.500 mg. of strontium nitrate per gram body weight all mice died.

8) Following subcutaneous injection of less than 0.013 mg. of barium nitrate per gram body weight all mice survived. Some of the mice died following subcutaneous injection of more than 0.018 mg. of barium nitrate per gram body weight, and all mice died following subcutaneous injection of more than 0.020 mg. of barium nitrate per gram body weight.

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REFERENCES

1) Kawin, B., Copp, D. H., and Hamilton, J.G. : UCRL-812, 3, 1950.
2) Schubert, J.: Science, **105**, 389, 1947.
3) Schubert, J.: J. Lab. Clin. Med., **34**, 313, 1949.
4) Schubert, J. and Wallace, H., Jr. : J. Biol. Chem., **183**, 157, 1950.
5) Copp, D. H., Axelrod, D. J., and Hamilton, J. G.: Am. J. Roentgenol. Rad. Therapy, **58**, 10, 1947.
6) Cohn, S, H. and Gong, J. K.: Proc. Soc. Exp. Biol. & Med., **83**, 550, 1953.
7) Kikuchi, T., Wakisaka, G., Kono, T., Goto, H., Akagi, H., Yamamasu, T., and Sugawa, I.: Studies on the Metabolism of Fission Products II. Studies on the Metabolism of the Radioisotopes Contained in the Radioactive Ashes Obtained from the No. 5 Fukuryu Maru. Paper X, This issue, 1954.